

of weakness and paralysis of the vasoconstrictors. (2) Acceleration of the pulse due to the action of the toxin on the heart. (3) Large doses produced death of the animals, with restlessness, collapse, and dyspnea, and postmortem examination showed death from suffocation.

Sachsa⁶ injected a 10 per cent. watery solution into crural veins, and produced a fall in blood pressure, acceleration of the pulse, and death from acute suffocation. This toxic action was more marked in young animals. Both Svehla's and Sachsa's conclusions, that thymic asthma and thymic death may be due to hyperthymization of the blood, are in accord with my hypothesis.

On finishing this paper there came to my notice the research of Lucien and Parisot.⁷ These observers made a careful study of the influence of thymectomy in rabbits, and found that in very young animals removal of the thymus was followed by a noticeable retardation of growth. The changes in the skeleton were in the weight and general dimensions of bones; no curvatures, epiphyseal enlargements, or bony softening were found. The testicles and ovaries were diminished in size, corresponding with the lack of development of the organism in general. All of these changes were less noticeable in older animals, and did not occur at all in animals that had attained their full development. These findings of Lucien and Parisot may be explained by the hypothesis above advanced.

A CASE OF SPLENOMEGALY ASSOCIATED WITH MARKED ANEMIA OF THE PERNICIOUS TYPE.

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THE following case seems worthy of being put on record, as it presents many unusual features. The patient has been under observation in London and Toronto during many years, and the history can thus be followed out in a way that is often not possible. The diagnosis offers many difficulties, but if, as seems probable, it be one of pernicious anemia, with a very large spleen, then in several ways it is a case of great rarity.

W. P., aged twenty-eight years and six months. Single. Lead glass worker. Admitted to the Toronto General Hospital on June 12, 1909.

⁶ *Centralbl. f. allg. Path. u. path. Anat.*, 1897.

⁷ *Archiv. méd. exper. et d'anat. path.*, January, 1910.

Complaints. Weakness, shortness of breath on exertion, and swelling of the abdomen.

Duration. About four weeks, but, as the history will show, he has not been really well for at least twenty years.

Family History. Father alive and well. Rheumatism four times. Mother alive but delicate. Brothers, two; one died of whooping-cough; one healthy. Sisters, none. No history of tuberculosis or syphilis in the family. No history of any disease resembling what the patient now suffers from.

Personal History. Born in London, England. Came to Canada many years ago. Has been a lead glass worker for years. Fairly comfortable surroundings and always has good food. No venereal history.

Previous Health. Was a small, weakly baby. Had measles at the age of four. When eight years old was in the Great Ormond Street Hospital suffering from "jaundice," and remained there four months. (Notes of this stay are not obtainable.)

At ten years of age was readmitted to the Great Ormond Street Hospital, March 5, 1890, complaining of headache and dull abdominal pain. A summary of his condition then, as given by Mr. R. S. Frew, the Registrar to the hospital, is as follows: "Very thin boy. Skin pale lemon color. Conjunctivæ slightly tinged. No eruptions or œdema. Lips pale and gums slightly swollen. Tongue pale. Cervical glands enlarged, especially on the left side. Temperature, 101°. Abdomen not distended. Prominence in left hypochondrium reaching to umbilicus and descending on respiration. Spleen reaches to within 1½ inches of left anterior superior iliac spine. Notch in its anterior border evident. Liver palpable below costal margin. Heart not enlarged, but systolic murmurs in all areas, conducted into axilla. Chest normal. Blood: Red cells, 1,000,000, white cells, 18,000, hemoglobin, 12 per cent.; March 25, hemoglobin, 25 per cent.; April 1, red cells, 1,625,000, white cells, 26,625, hemoglobin, 25 per cent.; April 17, red cells, 1,100,000, white cells, 7750, hemoglobin, 40 per cent.; April 28, red cells, 1,700,000, white cells, 10,000, hemoglobin, 40 per cent. Blood smear normal. Diagnosis, enlarged spleen."

Was readmitted in September, 1890 (aged ten years and nine months). "Since discharge had gradually become short of breath; lost color; had pains in head and abdomen; no hemorrhages nor vomiting. He was yellowish in color. Temperature, 100°. Glands enlarged along posterior border of sternomastoid, and shotty in left groin. Elsewhere were normal. Spleen was much enlarged. Liver not palpable. Systolic murmurs as before. Urine contained no albumin or sugar. Blood: Red cells, 1,111,000; white cells, 10,000; hemoglobin, 25 per cent.: September 17, red cells, 2,900,000; white cells, 10,000; hemoglobin, 46 per cent.: October 13, red cells, 3,500,000; white cells, 14,000; hemoglobin, 70 per cent. Optic disks normal. Sent to Convalescent Home."

February 9, 1891. "Reported at the out-patient department. Is paler again. No pain. Spleen reaches to one inch beyond the umbilicus. Blood: Red cells, 700,000; white cells, 21,200; hemoglobin, 19 per cent. After that was twice at the Great Ormond Street Hospital as an in-patient at short intervals. The condition was much the same, and he always temporarily improved."

The patient next turned up at St. Mary's Hospital, under the care of Dr. (now Sir) John F. H. Broadbent, who writes that he well remembers the case; and we are indebted to Dr. M. Mitchell Bird, the medical superintendent of the hospital for further notes, which are condensed to the following: The patient was admitted on July 23, 1894, then aged fourteen years. He complained of dyspnoea, anemia, slight cough, and extreme weakness. He stated that his periods of good health had been longer after each course of treatment at the Great Ormond Street Hospital. Had been fairly well before the present attack. He was of a pale yellow color. Spleen much enlarged. Liver palpable below the costal margin. Loud systolic murmurs audible all over precordium. Blood: Red cells, 800,000; white cells, not increased; hemoglobin, 25 per cent. He was treated with rest, arsenic, and iron, and left the hospital much improved.

During the next fourteen years of his life the patient says that he has been well and has never been laid up nor required medical advice. About a month ago, however, his old symptoms of weakness, dyspnoea, and yellow pallor returned, and he has been very poorly since. A week ago he fainted. He entered the Toronto General Hospital on June 4, 1909.

Condition on Admission. Patient is a well-developed man. Skin has a yellow and pallid hue and the conjunctivæ are distinctly jaundiced. In the folds of the axillæ and elsewhere there is considerable pigmentation. He gives a negative Moro reaction. Temperature, 100.3°, and all through his stay in the hospital there was slight elevation of the temperature. The lymphatic glands on the right side of the body are slightly enlarged. (The enlargement was on the left side in boyhood according to the records.) There is no tenderness over the long bones. No wrist-drop or trophic changes suggestive of lead poisoning.

Alimentary System. The teeth are poor and carious. The spleen is greatly enlarged and reaches to half an inch beyond the umbilicus. It is firm and free from tenderness. The notch is very evident and there is a slight shallow groove across the surface of the organ. The liver is not enlarged. The stools are somewhat clay-colored.

Circulatory System. Some dyspnoea and faintness on exertion. He can lie down in bed. No œdema or cyanosis. Pulse is regular and of medium systolic pressure, but collapses between the beats, almost suggesting a "water-hammer" one. The heart is not evi-

dently enlarged. Systolic murmurs are audible all over precordium and there is a loud *bruit du diable* in the neck. There is a slight retraction at the right apex, but otherwise the respiratory system seems normal.

Urine. Quantity normal. Dark red in color, but does not give the bile reaction with nitric acid. A trace of albumin. No indican. Many crystals of calcium oxalate, uric acid, and urates.

Nervous system normal. Nothing abnormal in *fundi oculorum*.

Blood. Shows a marked anemia of the pernicious type, in that the color index was persistently 1 or above. The results of the frequent examinations are collated in the following table:

BLOOD EXAMINATIONS.

Date.	Hemoglobin.	Red blood cells.	White blood cells.	Nucleated red blood cells.	Differential Counts.	Polynuclears.	Eosinophiles.	Basophiles.	Lymphocytes.		Normoblasts.	Megaloblasts.	Total nucleated red blood cells.
									Large.	Small.			
1909													
June 12	28	1,152,000	28,000	10,890		65.40	1.57	1.57	3.77	27.67	11.31	27.60	38.91
June 13	..	1,440,000	25,700	13,261		65.00	2.00	0.60	5.80	26.40	22.25	29.35	51.60
June 14	26		23,900	9,010		63.30	1.60	0.60	7.30	27.20	17.70	20.00	37.70
June 15	28	1,520,000	18,000	5,997		63.70	3.20	1.60	4.16	27.20	16.33	17.00	33.00
June 16	31	1,750,000	14,800	5,097		58.36	4.73	1.26	5.04	36.00			34.44
June 17	34	1,724,000	14,000	5,250		60.00	1.90	2.52	32.70				34.44
June 18	38	1,824,000	16,000										
June 19	40	1,856,000	12,000	3,624		62.42	3.18	2.20	4.80	27.07	12.40	17.80	30.20
June 20	40	2,018,000	14,800	5,772		55.60	2.50	1.20	3.20	37.30	12.90	26.10	39.00
June 21	..	2,800,000	18,000	7,560		60.10	1.60	2.20	5.10	30.87	14.80	27.30	42.10
June 22	41	2,280,000	11,600										
June 23	45	2,180,000	12,000	3,345		61.50	3.54	1.60	3.50	30.00	8.33	10.55	27.88
June 24	45	2,204,000	14,000	2,261		70.90	1.60	1.30	4.00	22.29	5.45	10.70	16.15
June 26	45		11,600	2,784		65.70	1.60	0.60	6.70	25.30	7.00	17.00	24.00
June 29	46	2,300,000	11,600	1,032		67.50	2.00	1.00	3.20	26.30	3.80	5.10	8.90
July 2	48	2,600,000	11,200										
July 6	50	2,964,000	11,300	247		62.00	3.00		6.50	28.50	2.50	2.00	4.50
July 9	46	2,890,000	5,500										
Nov. 28	..					64.50	4.50	1.50	3.00	26.00	0.50	1.00	1.50
1910													
Feb. 13	..					74.20	5.80	1.00	4.50	14.50	0.30	1.30	1.60

The white cells showed marked signs of immaturity or a tendency to degeneration. Some large mononuclear forms seemed closely to resemble myelocytes, but their structure was too definite. Many of the polymorphonuclears were very small, and a tendency to acid staining was evident.

The chief change in the blood was in the red cells. Fully 50 per cent. of the non-nucleated forms showed staining in an atypical bluish tint. Stippling was marked, varying from a few coarse blue granules to hundreds of coarse or fine ones, so closely packed as to produce a close resemblance to an atypical white cell. The question naturally arises here of whether the lead-working occupation of the patient had anything to do with this, but as both in pernicious anemia and in splenic anemia such staining is common,

this suspicion loses much of its weight. The poikilocytosis of the non-nucleated forms was mainly in regard to size, although many cells were irregular in outline and even rosette in form. Some of them were very large.

Many cells were so destitute of staining as to appear as mere ghosts, with just a faintly staining outline.

The nucleated red cells were exceedingly variable in form. The majority of them showed a primitive form of nucleus with a definite chromatin network and frequently more than one nucleolus. They answer very closely to the appearance of bone marrow, or lymphoid cells, which, according to many are the mother cells alike of the red and most of the white corpuscles. These cells not infrequently showed mitotic figures. The other nucleated red cells showed a uniformly intensely blue staining nucleus, or several nuclei, up to seven; an atypical budding process appearing in some cases. Free nuclei of this description were frequently noted in the smear, some just becoming detached from the cell body. These nuclei made the differentiation of lymphocytes a difficult matter. The majority of the nucleated red cells were megaloblasts, though normoblasts and some microblasts were present.

The smears were made on slides, stained by Wright's usual technique, and were counted under a Zeiss $\frac{1}{2}$ oil-immersion lens. The cells were counted by the same Thoma-Zeiss hemocytometer throughout.

The hemoglobin was estimated by two separate readings with the Dare hemoglobinometer.

Smears made by the patient at his home in November and February last showed more regularity in size and shape of the red cells, but still many nucleated forms. The color index as mentioned was always 1 or above 1.

During his stay in the hospital the patient improved greatly, he rapidly gained strength, his jaundice disappeared, and the spleen became rather smaller.

On February 13 last he writes that he thinks that his spleen is down to its normal size, and that he feels as well as he ever did in his life. This letter was of the same date as the last smear in the table, in which the still abnormal condition of the blood is evident.

REMARKS. The blood picture alone would suggest a diagnosis of pernicious anemia; the marked number of nucleated red cells and especially the great proportion of megaloblasts making it probable that we had to deal with the plastic form of this disease. The splenomegaly, although being unusual in pernicious anemia, would by no means exclude it, as cases are on record in which the spleen was quite as big as in our case, in which the disease was undoubtedly of the pernicious type. Osler records such a case, which was at first taken to be one of splenic anemia, but subsequently came to

postmortem and proved to be one of pernicious anemia,¹ and in something like 1 per cent. of all cases of pernicious anemia the spleen is so large as to reach to the umbilicus.² But assuming for the moment that the case be one of pernicious anemia, even then it presents several most unusual features. In the first place the disease commenced at the age of eight years, if not earlier, which is very unusual. Again, it has lasted for at least twenty years, and the patient is still in comparatively good health; and yet the longest cases recorded, apart from six cases of apparent recovery, only lasted between fourteen and fifteen years (Cabot³). Further, according to the patient's history, he was so well between the ages of fourteen and twenty-eight that he was never laid up nor required any medical advice—that is, he seemed to have a remission of fourteen years, and yet the longest recorded remission from prostrating symptoms on record is six years,⁴ although McPhedran⁵ recently has reported a case in which there was a remission for seventeen years.

As regards splenic anemia, the enormous size of the spleen with the marked anemia and a normal differential white blood count would superficially suggest such a diagnosis, but the very profoundness of the anemia would be against this conclusion, and further, the fact that the anemia was always of the pernicious form with a high color index would seem to exclude this diagnosis.

Other forms of splenomegaly with anemia, such as congenital syphilis, tumor, malaria, and even a possibility of filaria were all carefully weighed and excluded.

The case would appear to be either one of pernicious anemia of an exceptionally prolonged type, commencing at an exceptionally early age, and associated with an exceptionally large spleen, or one of splenic anemia with an exceptional blood picture.

The patient has left Canada for the United States, and we hope that his condition may be followed out by whomsoever he may consult.

¹ Transactions of the Association of American Physicians, 1902.

² Osler's Modern Medicine, iv, 765.

³ Ibid., 635.

⁴ Ibid., 633.

⁵ Amer. Jour. Med. Sci., 1910, cxi, 261.

THE SPINAL CORD LESIONS IN TWO CASES OF PERNICIOUS (ADDISONIAN) ANEMIA.

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THE following cases of spinal cord lesion with anemia belong to that group first described by Lichtheim¹ in 1887, and by many observers since, such as Bastianelli², Burr,³ Clarke,⁴ Jacob,⁵ Jacob and Moxter,⁶ Lenoble,⁷ Putnam and Taylor,⁸ Russel,⁹ Nonne,¹⁰ and especially by Putnam¹¹ and Dana¹² in this country, and recently termed by certain German observers pseudocombined sclerosis. The two patients whose records are presented were under the independent observation of several clinicians in three large hospitals of New York: Drs. W. Gilman Thompson, W. B. Pritchard, L. A. Conner, and T. W. Hastings, to whom we are indebted for the early records, extending back in one case three years, in the other five years. The first case we saw in Dr. Pritchard's service in the City Hospital, and the second case was under the personal observation of one of us for a year in the Cornell Dispensary and the City Hospital.

CASE I.—Under observation five years; symptoms and signs of pernicious anemia; no neurological features; at the postmortem the characteristic changes of pernicious anemia; in the cord, from the

¹ Zur Kenntniss der im Verlaufe der perniciosen Anämie, etc., Verhandl. des VI Congress f. innere Med., Wiesbaden, 1887, p. 84.

² La sclerosi combinale de midollo spinale nelle anemie perniciose, Bulle. Roy. Acad. di Roma, 1895-96, xii.

³ The Spinal Cord Lesions and Symptoms of Pernicious Anemia, Univ. Med. Mag., 1895, vii, 472.

⁴ Remarks on the Changes in the Spinal Cord in Two Cases of Pernicious Anemia, Brit. Med. Jour., 1897, ii, 325; On the Spinal Cord Degeneration in Anemia, Brain, 1904, xvii, 441.

⁵ Rückenmarkserkrankungen bei letaler Anämie, Fortschr. d. Med., xv, 569.

⁶ Über Rückenmarkserkrankung und Veränderungen bei tödlich verlaufenden Anämien, Deut. med. Woch., 1898, xxiv, 152.

⁷ Contribution à l'étude des lésions médullaires dans l'anémie perniciose progressive protopathique, Rev. de méd., 1897, vi, 425.

⁸ Diffuse Degeneration of the Spinal Cord, Jour. Nerv. and Ment. Dis., 1901, xxxviii, i, 74.

⁹ The Relation of Some Forms of Combined Degeneration of the Spinal Cord to one Another and to Anemia, Lancet, 1898, ii, 4.

¹⁰ Klinischer und anatomischer Beitrag zum Capitel der Prognose der anämischen Spinalerkrankung—2 Fälle von anämischer Spinalerkrankung mit Dissociation der Anämie und des Spinalleidens, Mittheilung aus der Hamburgischen Staatsanstalten, 1907, ii, 1 to 7.

¹¹ A Group of Cases of System Sclerosis of the Spinal Cord Associated with Diffuse Degeneration; Occurring in Enfeebled Persons, Past Middle Life, and Especially in Women; Studied with Particular Reference to Etiology. Jour. Nerv. and Ment. Dis., 1891, xviii, 69.

¹² The Degenerative Diseases of the Spinal Cord, with the Description of a New Type, Jour. Nerv. and Ment. Dis., 1891, xviii, 205; Subacute Combined Sclerosis of the Spinal Cord and its Relation to Anemia and Toxemia, Jour. Nerv. and Ment. Dis., 1899, xxvi, 1.